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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,236	12/12/2001	John Andrew Ryals	PB/5-21215C	4030

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EXAMINER	
KUBELIK, ANNE R.	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 08/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,236	RYALS ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,10,42,58,59,62 and 68-93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 8, 10, 42, 58-59, 62 and 68-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. As requested in the preliminary amendment filed with the application, claims 2-7, 9, 11-41, 43-57, 60-61 and 63-67 have been cancelled, claims 1, 8, 10, 42, 58-59 and 62 have been amended, and claims 68-93 have been added. Claims 1, 8, 10, 42, 58-59, 62 and 68-93 are pending.

2. The draftsman has approved the drawings as submitted.

3. The abstract is not descriptive of the instant invention, which is a method for protecting plants by transformation with a NIM1 gene and by applying a microbiocide. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

4. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

5. The priority claim in the first paragraph of the specification is incomplete. Parent Application 08/996,685 is a continuation-in-part of US Application 08/761,543, filed 6 December 1996, now US Patent 5,780,489, a continuation-in-part of US Application 08/875,015 and a continuation-in-part of PCT/EP96/02672. The first paragraph of the specification should be amended to reflect this. Additionally, the declaration indicates that the instant application claims benefit of US Application 08/981,575 and of PCT/EP96/00096; these claims should be recited in the first paragraph of the specification, along with the relationship (divisional,

continuation, continuation-in-part, or national stage) to the instant application or to its priority applications, as appropriate.

6. The disclosure is objected to because of the following informalities:

The Table of Contents on pages i-v should be deleted.

Claim Objections

7. Claims 8, 10, 42, 58-59, 62 and 68-93 are objected to because of the following informalities:

Claims 8, 10, 42, 58-59, 62 and 68-93 have an improper article at the start of the claims.

In claim 42, "following group" should be replaced with --group consisting of--.

In claim 93, the colon should be deleted.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 93 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "wherein the plant is ... chili" 3. Thus, such a phrase constitutes NEW MATTER.

In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

10. Claims 1, 42, 58-59, 62 and 68-93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid encoding SEQ ID NO:2 or of SEQ ID NO:1, does not reasonably provide enablement for a method of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid that hybridizes to SEQ ID NO:6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid that hybridizes to SEQ ID NO:6.

The instant specification, however, only provides guidance for testing the effectiveness of various microbiocides for preventing fungal attack on plants (examples 1-13), identification of cim3 mutant Arabidopsis plants that accumulate PR-1 during normal growth (example 14-16), evaluation of cim3 plants for resistance to fungal and bacterial pathogens (example 17), production of cim3nahH plants to determine that the two genes are epistatic to one another (example 18). The specification also provides guidance for testing the effectiveness of various microbiocides for preventing fungal attack on *cim3* plants (example 19), generation of plants transformed with nucleic acids encoding the IkB homolog NIM2 (SEQ ID NO:1 or 6) (examples 20-23), generation of altered forms of NIM1 that have two amino acid substitutions (SEQ ID

NO:8), an N-terminal deletion (SEQ ID NO:10), a C-terminal deletion (SEQ ID NO:12), both N-terminal and C-terminal deletions (SEQ ID NO:14), or consist only of ankyrin domains (SEQ ID NO:16 (examples 24-28), putative transformation of them into *Arabidopsis* (examples 29-30), putative transformation of *cim3* plants with the NIM1 gene (example 31), and a method of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with SEQ ID NO:1 (example 34). The specification also provides general guidance for isolation of NIM1 homologs from other plants (example 32) and general guidance for transformation of plants with these homologs (example 33).

The instant specification fails to provide guidance for the sequence of any nucleic acid that hybridizes to SEQ ID NO:6 other than SEQ ID NO:1.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain signal transduction activity of the encoded protein.

While the specification teaches that SEQ ID NO:2 has homology to IκBα, using protein homology to make amino acid substitutions is unpredictable. Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original proteins.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids that hybridize to SEQ ID NO:6. Making all possible single amino acid substitutions in an 594 amino acid long protein like that encoded by SEQ ID NO:6 would require making and analyzing 19^{594} nucleic acids; these proteins would have 99.8% identity to SEQ ID NO:2. Because nucleic acids that hybridize to SEQ ID NO:6 under low stringency conditions would encode proteins with many amino acid substitutions, many more than 19^{594} nucleic acids would need to be made and analyzed.

SEQ ID NO:6 encodes a NIM1/NPR1 protein. Not all NPR1 variants would confer disease resistance to plants that had been transformed with the gene that encode them. *Arabidopsis nim1* mutants support the growth of normally incompatible races of a fungal pathogen, and are thus, less resistant to disease than wild-type plants (Delaney et al, 1995, Proc. Natl. Acad. Sci. USA 92:6602-6606, see pg 6604, left column, paragraph 1 and right column paragraph 4). Plants transformed with a *nim1* gene would not be more resistant to disease than nontransformed plants, even though *nim1* would still be "involved" in the signal transduction cascade leading to systemic acquired resistance. The *nim1* mutants differ from the wild-type *NIM1* gene by a single base (Ryals et al, 1997, Plant Cell 9:425-439). Thus, not all nucleic acids that hybridize to SEQ ID NO:6 would confer resistance to a plant into which they had been transformed.

As the specification does not describe the transformation of any plant with a nucleic acid that hybridizes under low stringency conditions to SEQ ID NO:6, other than SEQ ID NO:1, undue trial and error experimentation would be required to screen through the myriad of nucleic

acids encompassed by the claims and plants transformed therewith, to identify those with disease resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

11. Claims 1, 42, 58-59, 62 and 68-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to use of a multitude of DNA molecules that hybridize to SEQ ID NO:6, wherein the nucleic acid encodes a protein involved in the signal transduction cascade leading to systemic acquired resistance in plants. In contrast, the specification only describes the coding sequences, SEQ ID NO:1 and 6, for the Arabidopsis protein SEQ ID NO:2. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

The description of the function of the encoded protein, that is, a protein "involved" in the signal transduction cascade leading to systemic acquired resistance in plants, does not specifically describe the function of the protein. What is the nature of the involvement in the signal transduction cascade? Does it bind the signal on the outside of the cell? Does it pass the signal from one protein to one or more other, and if so what are those other proteins? Is it the transcriptional activator or repressor or pathogenesis-related protein at the end of the cascade?

Because the sequences are not described, the method of using the sequences to protect plants from pathogen attack is likewise not described to the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 8, 10, 42, 58-59, 62 and 68-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is indefinite in its recitation of "involved in the signal transduction cascade leading to systemic acquired resistance". The nature of that involvement is unclear.

Claim 1 is indefinite in its recitation of "(X3)", "(X1)" and "at 55°C" in lines 9-10. Does "(X3)" and "(X1)" describe the number of times each wash is done? Which wash is at 55°C? - the 6XSCCC one or the 3XSCCC one?

Claim 93 is indefinite in its recitation of "plant is ... chili". Chili is not a plant. Does Applicant mean a pepper plant?

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1, 8, 10, 42, 58-59, 62 and 68-93 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,031,153. Although the conflicting claims are not identical, they are not patentably distinct from each other because methods of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid encoding SEQ ID NO:2 or of SEQ ID NO:1, as claimed in the issued patent, is a species of the genus of methods of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid that hybridizes to SEQ ID NO:6, as claimed in the instant application. Furthermore, SEQ ID NO:6 is

the cDNA that encodes SEQ ID NO:2. The microbiocides used in the method of the issued patent and the same microbiocides use din the method of the instant application.

16. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

17. Claim 8 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 6,031,153. This is a double patenting rejection.

18. Claims 1, 8, 10, 42, 58-59, 62 and 68-93 are free of the prior art, given the failure of the prior art to teach or suggest a method of protecting plants from pathogen attack by applying a microbiocide to a plant transformed with a nucleic acid that hybridizes to SEQ ID NO:6 and that encodes a protein in the signal transduction cascade leading to systemic acquired resistance.

Conclusion

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
August 14, 2003

AMY J. NELSON, PH.D
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